

### **REMARKS**

Claims 1-28 were pending in the application. Claims 1, 2 and 8 have been amended. Therefore, claims 1-28 remain pending.

No new matter has been added. Support for the amendments to claims 1 and 2 can be found, for example, at least at page 5, lines 5-11 of the specification as originally filed.

#### ***Amendments to the Specification***

The Examiner suggests that Applicants amend the specification to incorporate the patent number of the parent application. Accordingly, Applicants have amended the specification as suggested.

#### ***Provisional Rejection of Claims 1 and 2 Under the Statutory Type (35 U.S.C. §101) Double Patenting***

The Examiner has provisionally rejected claims 1 and 2 under 35 U.S.C. § 101 as “claiming the same invention as that of claims 1 and 2 of copending Application No. 11/004,559.”

Applicants respectfully submit that the aforementioned rejection of the claims 1 and 2 has been rendered moot in view of the amendments to the claims. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection of the claims.

#### ***Provisional Rejection of Claims 3-28 Under the Doctrine of Obviousness-Type Double Patenting***

The Examiner has provisionally rejected claims 3-28 under the judicially created doctrine of obviousness-type double patenting as “being unpatentable over claims 3-13 of co-pending Application No. 11/004,559.” The Examiner is of the opinion that “[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the ‘559 application anticipate the instant claims.”

Applicants respectfully submit that, while in no way admitting that the present claims are obvious over claims 3-13 of co-pending Application No. 11/004,559, upon allowance of the ‘559 application, Applicants will consider submitting a terminal disclaimer in compliance with 37 C.F.R. 1.321(b) and (c), if appropriate, which will obviate the rejection.

#### ***Rejection of Claim 8 Under 35 U.S.C. § 112, first paragraph***

Claim 8 is rejected under 35 U.S.C. § 112, first paragraph for failing to comply with the written description requirement. Specifically, the Examiner states that “[t]he instant claim recites organic substituents precursors and ‘their derivatives’” and that the “present specification lacks

definition and working examples of what applicant intends by the term 'derivatives'."

Applicants have amended the claim to delete the phrase "and their derivatives" as suggested by the Examiner. Therefore, Applicants respectfully submit that this rejection no longer applies to claim 8 and request that this rejection of the claim under 35 U.S.C. § 112, first paragraph, be withdrawn.

***Rejection of Claim 8 Under 35 U.S.C. § 112, second paragraph***

Claim 8 is rejected under 35 U.S.C. § 112, second paragraph as "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Specifically, the Examiner states that "the language of the instant claim is unclear because of the recitation of the term 'derivatives'."

Applicants have amended the claim to delete the term "derivatives." Therefore, Applicants respectfully submit that this rejection no longer applies to claim 8 and request that this rejection of the claim under 35 U.S.C. § 112, second paragraph, be withdrawn.

***Rejection of Claims 1-3, 7 and 8 Under 35 U.S.C. § 102(b)***

Claims 1-3, 7 and 8 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Esse *et al.* (U.S. Patent No. 3,609,188). Specifically, the Examiner states that "Esse *et al.* teach the production of 4-substituted tetracyclines by contacting 4-hydroxytetracycloxide with a primary lower alkyl amine or alkanolamine and a metal catalysts such as palladium, platinum or rhodium catalyst." The Examiner also asserts that "[t]he process taught by the reference is encompassed by the instant claims."

Applicants respectfully submit that the claims, as amended, teach methods of making 7-, 9- or 13-substituted tetracycline compounds by contacting a reactive tetracycline-based precursor compound with a transition metal catalyst forming a reactive chemical intermediate with a reactive organic substituent precursor such that a 7-, 9-, or 13-substituted tetracycline compound substituted with the organic substituent is formed. The reactive organic substituent precursor is defined in the specification, at least at page 8, lines 6-14, as including  $\pi$ -bonded species such methylene compounds, aryl boronic acids, active aromatic rings and unsubstituted and substituted olefins and alkynes, nitriles, acetylenes, substituted acetylenes, arylenes, styrenes, conjugated dienes, isoprenes, vinyl ethers,  $\alpha$ ,  $\beta$ -unsaturated aldehydes and ketones, aryl vinyl and arylisoprenyl ketones, iodoalkenes and iodoarenes, quinones,  $\alpha$ ,  $\beta$ -unsaturated acids and their derivatives.

Esse *et al.* teaches 4-substituted tetracycline compounds prepared by contacting a 4-hydroxytetracycloxide with a primary lower alkyl amine or alkanolamine and a metal catalyst such as palladium, platinum or rhodium catalyst. Esse *et al.* does not teach or suggest methods of

making substituted tetracycline compounds by contacting a reactive tetracycline-based precursor compound in which the 7-, 9- or 13-position on the tetracycline compound is the reactive position. Furthermore, *Esse et al.* does not teach or suggest contacting such reactive tetracycline-based precursor compounds with a transition metal catalyst forming a reactive chemical intermediate with a reactive organic substituent precursor where the reactive organic substituent precursor is defined as a  $\pi$ -bonded species. In addition, *Esse et al.* does not teach or suggest 7-, 9-, or 13-substituted tetracycline compounds that are substituted with an organic substituent obtained from the a reactive organic substituent precursor. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw this rejection of the claims under 35 U.S.C. §102(b).


### SUMMARY

Amendments to the claims should in no way be construed as acquiescence to any of the Examiner's rejections. The amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. The amendments made to the claims are not related to any issues of patentability.

It is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conference with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

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